The impact of the COVID-19 pandemic on skin cancer incidence and treatment in England, 2020

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Dear Editor, The first UK national COVID-19 lockdown began on 23 March 2020. Immediately, almost all outpatient healthcare service requests temporarily focused exclusively on urgent referrals and 2-week-wait urgent cancer referrals, with restrictions due to staff sickness, redeployment and changing work environments. Additionally, patient anxiety regarding attending appointments and perceived overburdening of healthcare resources resulted in fewer presentations.[1]

Technological advancements have arisen from challenging circumstances. The National Cancer Registration and Analysis Service (NCRAS), England, has developed a Rapid Cancer Registration Dataset (RCRD). Due to automated data feeds, lag time from diagnosis to registration has been reduced from 18 to 4 months; however, data have not been quality assured to the same standards and completeness.[2,3] We identify how the pandemic has affected skin cancer.

The RCRD[2,3] provides estimates of cancer incidence using data from January 2018 to November 2020. The main resource is multidisciplinary team meeting datasets, which are not a reliable source for basal cell carcinomas (BCCs) and cutaneous squamous cell carcinomas (cSCCs), effectively excluding them. RCRD tumour resection procedures are identified as a definitive treatment, for example an excision but not a diagnostic biopsy.

A separate tool to identify BCC and cSCC pathology reports received by NCRAS before registration was developed for quality assurance; it was not developed to report incidence and so should be interpreted cautiously.[4] Pathology reports duplicate tumours when there are diagnostic biopsies, re-excisions, recurrences and supplementary reports. Furthermore, these data have not been quality assessed and therefore they are best interpreted as a representation of workload rather than incidence. The date of the report used is the date of sample collection preferentially.

Both methods are crude and not the gold standard of tumour registration. Therefore they are not representative of the true incidence but are rather an early, rapid estimate. All reported proportions represent a comparison of the same month or period of the previous year.

In May 2020, melanoma diagnoses reduced to 54%, increasing to 83% by November 2020. During the 8-month period from April 2020 to November 2020, melanoma diagnoses reduced to 72%, with 2671 fewer melanomas diagnosed. Likewise, a reduction was seen in the diagnosis of all malignant cancers (excluding nonmelanoma skin cancer, NMSC) (74%), prostate cancer (64%), breast cancer (73%) and lung cancer (88%) over the same period (Figure 1a). The proportion of resection procedures in May 2020 fell to 69%, with an increase to 87% by November 2020 (Figure 1b). Cancer Waiting Times first treatments for melanoma similarly fell to 58% in May 2020 and rose to 91% by December 2020 (Figure 1c). Pathology reports for cSCCs and BCCs in April 2020 fell to 58% and 22%, respectively. By September 2020 counts increased to 95% for cSCCs and 72% for BCCs (Figure 1d).

Undoubtedly, fewer cancer diagnoses are being made during the pandemic and an incomplete rebound is seen. Melanoma incidence decreased more than the incidence of all cancers overall (excluding NMSC); however, it is comparable with that of other cancers. BCCs are typically downgraded to routine pathways once diagnosed unless considered high risk, and therefore BCC pathology report counts drop substantially more than for cSCC.

Comparatively, as a proportion of activity for the same month of the previous year, in Australia, a reduction in surgical procedures to 82% for cSCC and BCC, and 75% for melanoma was seen at the pandemic onset, with a more rapid recovery.[5] In Ontario, Canada, cSCC and BCC biopsies reduced to 82% and melanoma biopsies to 73% at the onset of the pandemic, with improvements seen in the following 10 weeks.[6] In a study of 143 US practices, melanoma diagnoses fell to 30·4%, SCCs to 22·3% and BCCs to 14·1% in April 2020, but have since improved.[7] Overall, a less substantial reduction in services is seen in countries where COVID-19 counts remained lower.

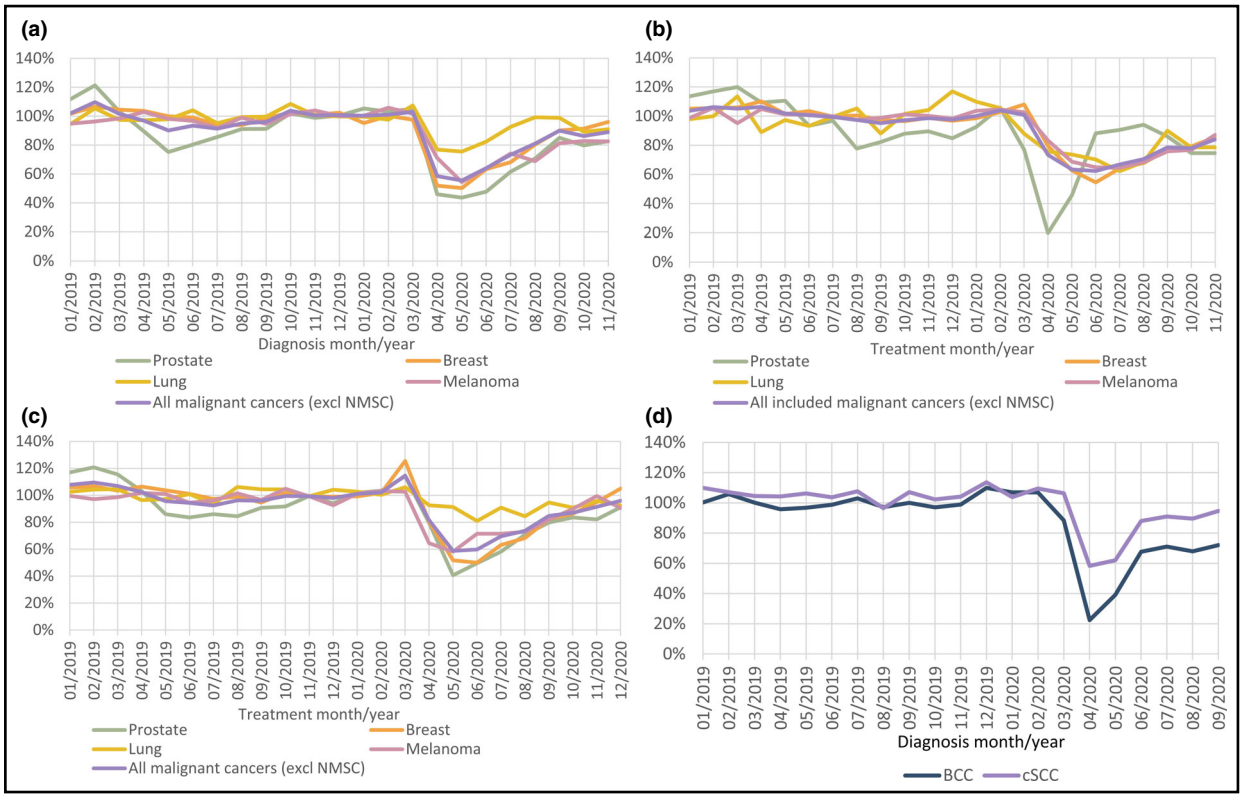

Figure 1 (a) Cancer diagnoses by cancer group and month, Rapid Cancer Registration Dataset (RCRD), England; working-day-adjusted. (b) Proportion of tumour resection procedures, by cancer group and month, RCRD, England. (c) First treatments by cancer group and month, Cancer Waiting Times data, England; working-day-adjusted. (d) Basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) pathology reports received at the National Cancer Registration and Analysis Service, CancerStats2 keratinocyte cancer report, England. All data are comparisons with the same month in the previous year. NMSC, non-melanoma skin cancer.

The main limitation of these data is the lack of standard quality assurance as a result of attaining more rapid access to data. NCRAS report that the RCRD melanoma data reported in Figure 1(a) record 13% false negative (missing) and 9% false positive (additional) compared with formally registered cases in 2018.[2,3] Although crude, these data are essential to understanding the wider repercussions of the COVID-19 pandemic beyond those directly infected. Early concerns precipitated the 'help us, help you' National Health Service campaign in October 2020,[8] which promoted support for public access to healthcare services during the pandemic.

It is essential to ensure that skin cancer services continue, with virtual appointments playing an increasingly important role. It is of grave concern that the decline in cancer incidence represents patients who are likely to present later, resulting in worse morbidity and mortality outcomes. Further research must be undertaken to understand better the long-term healthcare consequences of the pandemic to ensure we are able to prepare for further COVID-19 waves and future national emergencies.

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Cutaneous squamous cell carcinoma is associated with Lynch syndrome: widening the spectrum of Lynch syndrome-associated tumours

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Dear Editor, Lynch syndrome (LS) is caused by a germline mutation in one of the mismatch repair (MMR) genes. Individuals with LS have an increased risk of developing colorectal and many other tumours including skin tumours.[1] Sebaceous neoplasms and keratoacanthomas are skin tumours associated with LS, also known as Muir–Torre syndrome.[2] For cutaneous squamous cell carcinoma (SCC), an association with LS has been suggested.[3–5] Recently, a 12-fold increased risk for sebaceous carcinoma and SCC has been described in individuals with LS compared with the Dutch general population at the age of 60 years.[6]

Our aim was to evaluate whether cutaneous SCC is part of the LS tumour spectrum by evaluating the MMR status of cutaneous SCCs diagnosed in a cohort of individuals with LS. Furthermore, we evaluated the concordance between MMR immunohistochemistry (IHC) and microsatellite instability (MSI) polymerase chain reaction (PCR) testing.

Cutaneous SCCs were identified within a cohort of 331 individuals with LS, with a proven germline mutation, from 194 families, derived from two Dutch hospitals (January 2000 to October 2016), as described previously.[6] The study was approved by the institutional review board of the Netherlands Cancer Institute (IRBm19-123).

Pathology reports and formalin-fixed paraffin-embedded tissues were obtained for histopathological reassessment. IHC was performed according to standard protocols on slides for MMR proteins for the Ventana immunostainer (Roche Diagnostics Limited, Burgess Hill, UK). The proteins studied were MLH1 (clone ES05; Agilent, Santa Clara, CA, USA), MSH2 (clone G219-1129; Roche), MSH6 (clone EP49; Epitomics, Burlingame, CA, USA) and PMS2 (clone A16-4; Roche). Cutaneous SCCs with absent staining of one or more MMR proteins were considered MMR deficient.

DNA was isolated using a Qiagen extraction kit (Qiagen, Venlo, the Netherlands). A pentaplex PCR-based assay for MSI was performed using fluorescent-labelled primers of five mononucleotide repeat targets (BAT25, BAT26, NR24, NR21 and NR27), followed by fragment analysis. MSI was defined as instability in two or more markers.

In 331 individuals with LS, in total 13 cutaneous SCCs were diagnosed in eight patients (2·4%) (11 SCCs as described earlier and two additional SCCs identified in 2015 and 2017 within this cohort). Tissue from 10 of these 13 cutaneous SCCs in seven patients was available for further analyses. Three patients were diagnosed with two SCCs each. Two patients were male (29%) and the majority were diagnosed with an *MSH2* germline mutation (86%; Table 1). Five patients had a history of dermatological neoplasms prior to SCC diagnosis. The median age at diagnosis of the first cutaneous SCC was 52 years (range 33–60).

MMR IHC and MSI PCR testing were performed in the 10 and nine available cutaneous SCCs, respectively (from one sample there was not enough DNA available). MMR deficiency was detected in all 10 cutaneous SCCs by IHC, with the deficiencies corresponding to the LS germline mutations. MSI PCR demonstrated MSI in three of nine cutaneous SCCs, resulting in a discordance of 67% between MMR IHC and MSI PCR. All of these three patients had two cutaneous SCCs, with both concordant and discordant results between MMR IHC and MSI PCR (Table 1).

We showed that all cutaneous SCCs diagnosed in individuals with LS were MMR deficient, with loss of staining of MMR proteins corresponding to the known germline mutation, suggesting that SCC is an LS-associated tumour. We assume that MMR-deficient cutaneous SCCs develop by a germline mutation in one of the MMR genes, followed by a second hit of the wildtype copy.

Concordance between MMR IHC and MSI PCR is high for colorectal and endometrial cancer, but a low concordance has been described for other (skin) malignancies.[7,8] Explanations can be that high tumour turnover is necessary to induce enough detectable MSI or that the standard pentaplex panel is not effective for all tumours.[8] Therefore, we suggest performing only MMR IHC to detect LS in cutaneous SCC.